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Published in:
Transplantation Proceedings

DOI:
[10.1016/S0041-1345\(97\)01367-5](https://doi.org/10.1016/S0041-1345(97)01367-5)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
1998

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

De Vos, P., Hillebrands, J.L., De Haan, B.J., Strubbe, J.H., & Van Schilfgaarde, R. (1998). An artificial transplantation site for pancreatic islets. *Transplantation Proceedings*, 30(2), 484-484.
[https://doi.org/10.1016/S0041-1345\(97\)01367-5](https://doi.org/10.1016/S0041-1345(97)01367-5)

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An Artificial Transplantation Site for Pancreatic Islets

P. De Vos, J.L. Hillebrands, B.J. De Haan, J.H. Strubbe, and R. Van Schilfgaarde

MICROENCAPSULATED islets still have their functional limitations.¹ Transplantation near blood vessels may improve the function.² An intraperitoneally located and prevascularized expanded polytetrafluoroethylene (ePTFE) solid support is potentially a suitable transplantation site for encapsulated pancreatic islets because it allows both for the implantation of a large volume islet graft in the immediate vicinity of blood vessels and for its complete removal. ePTFE seems a suitable material for the construction of solid supports as it is biocompatible³ and can be coated to induce vascularization.⁴ The present study investigates the efficacy of an ePTFE solid support for the implantation of nonencapsulated islet isografts in streptozotocin-induced diabetic rat recipients.

MATERIALS AND METHOD

Solid supports were prepared from expanded fibers of ePTFE (courtesy of W.L. Gore & Associates). Islet isografts were transplanted in streptozotocin-induced diabetic rat recipients 4 weeks after intraperitoneal implantation of the supports. Diabetic rats transplanted with islets in the unmodified peritoneal cavity served as controls. Recipients of successful grafts were provided with permanent cardiac catheters for blood sampling and infusion in undisturbed, freely moving rats.

RESULTS AND DISCUSSION

Solid supports were always coated with a-FGF because we found that this growth factor enhances the neovascularization. The success rates of 5- μ L (group A) and 10- μ L (group B) islet isografts in solid supports were compared to the success rates of 5- μ L (group C) and 10- μ L (group D) islet isografts implanted in the unmodified peritoneal cavity. Four of seven rats in group A and all seven rats in group B became normoglycemic for at least 6 months. Only two of eight rats in group C and 4 of 11 rats in group D showed normoglycemia, which lasted for at least 6 months in none of two in group C and three of four in group D. Because of the low success rates in groups C and D, intravenous and oral glucose testing were restricted to the successful recipients in groups A and B. Glucose tolerance was found to be proportional to the grafted islet volume but, expectedly,⁵ in both groups the glucose tolerance and the insulin responses were somewhat lower than in controls. Thus, the present results show that the prevascularized ePTFE solid support rather than the unmodified peritoneal cavity is an efficacious transplantation site.

The principle of grafting in solid support is also applicable for encapsulated islets which, as a consequence of its large volume, can only be transplanted in the peritoneal cavity as a nonvascularized, freely floating graft. However, the ePTFE solid support as used for nonencapsulated islets in the present study has to be modified to serve as a transplantation site for encapsulated islets because grafting between the ePTFE fibers was found to be associated with damage to the encapsulated islets via the following two mechanisms. Grafting in ePTFE solid supports requires preparation of multiple tunnels by puncturing.⁶ This puncturing is followed by a wound healing process which is associated with cytokine release and damage to the encapsulated islets. Second, and most importantly, we found that grafting of the capsules into the present support was associated with induction of imperfections onto the capsule surface which resulted in fibrotic overgrowth of the implanted capsules with ischemia, and necrosis of the encapsulated islets as a consequence. Probably, the closure of the punctures is associated with mechanical pressure on the capsules which induces breakage of the capsule membrane.

Our research now concentrates on creating a vascularized ePTFE support with an accessible hollow, chamber-like space that can serve as a transplantation site for encapsulated islets.

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